REMARKS

The Office Action of March 10, 2005 presents the examination of claims 14-33. The present paper amends claims 14, 16, 17, 22, 23, 32 and 33. The amendments to the claims are merely of an editorial nature and in no way affect the scope of the claims.

Information Disclosure Statement

The Examiner indicates that the Kigawa reference has been crossed through as it is a foreign language document and the only translation provided is of the abstract. JP 04-91790 is indicated as not considered because no translation at all has been provided.

Applicants first note that more than the abstract of the Kigawa reference was translated. In Applicants' opinion, the parts of the Kigawa reference relevant to patentability of the present claims were translated and that translation was provided. Nevertheless, to assure complete consideration of the Kigawa reference, Applicants provide attached hereto a complete translation of the Kigawa reference, together with an amended copy (to reflect the full translation) of the form PTO-1449 previously submitted. The Examiner is requested to consider the Kigawa reference and indicate that it has been duly considered on this new copy of the form PTO -1449.

Applicants again point out for clarification that EP0469610A1, which is published in English and has been considered by the Examiner, corresponds to JP 04-91790. Therefore, it is considered that no further submission of a translation of JP 04-91790 is necessary.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 14-33 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants submit that the presently amended claims address each of the concerns raised by the Examiner and therefore this rejection should be withdrawn.

In particular, references to a "first DNA fragment" have been clarified so as to make distinct whether a template or an amplification product is intended as the recited "fragment." The term "component" has been removed from claim 23.

In claim 22, the Examiner indicates that recitation of "a microorganism" comprising the template DNA to be amplified is vague because it is unclear how primers would enter the microorganism in order to work in the claimed amplification reaction. Applicants submit that one of ordinary skill in the art, to whom the claim is addressed, plainly understands that the microorganism would be one that is lysed, thereby rendering the template DNA accessible to primers for conducting an amplification reaction.

In claim 14, the Examiner indicates that the recited "terminal regions" are unclear as to their extent. Again one of ordinary skill in the art who reads the present specification understands that the specific number of nucleotides of overlap between the template and the primers is not important, so long as specific priming occurs. The Examiner might refer to Figure 1, which shows schematically the reactions described in the present claims. What is meant by "terminal regions" is very plain in view of this figure. To the degree that a linear template is amplified (claim 14) rather than a "DNA fragment cloned in a vector" (claim 17), the Examiner may visualize the portion of the circular DNA that is shown that lies between the left edge of the hatched box to the part above the arrow labeled "3' primer".

Rejections for lack of novelty

Claims 14-19, 21, 23-25 and 32-33 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lanar '949. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Claim 14 is also rejected under 35 U.S.C. § 102(b) as anticipated by Erlich '809 or under 35 U.S.C. § 102(e) as anticipated by Sorge '453. These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

In a first embodiment of the invention, described for example by claims 14, 15, 32 and the first amplification in claim 33, the template DNA is amplified to obtain the amplified DNA product in a single reaction mixture that utilizes two overlapping 5′ primers. On the other hand, each of Lanar and Sorge teaches using at least two different reaction mixtures in order to utilize both 5' primers. Furthermore, Sorge describes only extension at the 3' end of a template, not extension of both ends as in the present claims. Thus, the present invention is distinct from what is disclosed by these references and the rejections of claims 14 and 15, and claims dependent thereon, over Lanar or Sorge should be withdrawn.

Erlich fails to describe the overlapping arrangement of the two 5' primers, and also discloses only a nested amplification of a sequence within a target nucleic acid in a sample. Erlich does not disclose extensions at both 5' and 3' end of the target sequence encoding a protein of interest as in the present claims. Accordingly, the rejection of claim 14 over Erlich should also be withdrawn.

In further embodiments of the invention, for instance as set forth in claims 15, 17 and claims dependent thereon, 32 and in the second reaction of claim 33, one of the 5′ primers and the 3′ primer that are used are independent of the sequence of the cloned DNA to be amplified. Only one of the 5′ primers used includes a sequence that is dependent upon the sequence of the DNA template to be amplified. On the other hand, Lanar '949 describes an amplification reaction in which at least two primers, one of a 5′ primer and one of a 3′ primer, must be made in a manner specific to the sequence of the template being amplified.

Referring to Fig. 1 of the present application, the nucleotide sequence of 5' primer 1 used in the first PCR is not dependent on the sequence encoding a protein to be expressed. This sequence (marked with blue line) corresponds to 5' end of the first

DNA fragment and 3' end of the 5' DNA figment, as marked with blue line in the copy of Fig. 1 attached.

Similarly, the nucleotide sequence of 3' primer used in the first PCR is not dependent on the sequence encoding a protein to be expressed, because the sequence (marked with red line) hybridizes with a part of plasmid vector sequence. Therefore, sequences of both the 5' DNA fragment and the 3' DNA fragment are independent of the sequence encoding a protein to be expressed via amplification addition of transcription and translation signals, and optionally a tag sequence.

In the second PCR of the present invention, the 5' DNA fragment, 3' DNA fragment and universal primer are regarded as primers to amplify the first cloned DNA fragment encoding some protein, and these three primers can be used independently of the sequence to be amplified. If a variety of DNAs encoding different proteins are cloned into the same plasmid vector, in the present invention all of the DNA fragments encoding different proteins can be amplified using the same set of primers, i.e., the 5' DNA fragment, the 3' DNA fragment and the universal primer. Therefore, after the first PCR is carried out using only one gene-specific primer, 5' primer 2, and a common 3' primer, the subsequent second PCR can be performed using a common primer set that has expression regulatory sequences (a promoter, terminator, SD sequence etc.) and a optionally a tag sequence.

In contrast, referring to Fig 6 of Lanar '949, primer A contains both a universal promoter-specific sequence and a gene-specific sequence (see Fig. 5). Primer B also appears to be gene-specific. In step 3, the products of step 1 and step 2 are mixed with primer H3T7 and primer B (boxed reaction) and amplified in a two step PCR analogous to splicing by overlap extension, which corresponds to the second PCR of the present invention. Although a universal promoter links to a DNA sequence that can be transcribed and translated, there is no indication to prepare a lot of template simultaneously and efficiently with minimum number of primers. In the total

procedures from step 1 to step 3 in the method of Lanar '949, two kinds of primers A and B have to be synthesized that are specific for the particular template DNA being amplified.

Thus, the present invention as represented by claims 17 and claims dependent thereon is also distinct from what is disclosed by Lanar '949. Accordingly, the rejection of all of claims 14-19, 21, 23-25 and 32-33 under 35 U.S.C. § 102(b) over Lanar '949 should be withdrawn.

Rejection for obviousness

Claims 14-28, 30 and 32-33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lanar '949 in view of Rothschild '337. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the combination of references cited by the Examiner fails to establish *prima facie* obviousness of the invention. In particular, as explained above, Lanar '949 does not disclose or suggest that a template DNA fragment should be amplified using two overlapping 5' primers in a single reaction mixture. Neither does Lanar '949 disclose or suggest use of only one primer for the amplification that is specific for the template DNA being amplified. Rothschild is cited for disclosure that a sequence encoding a particular tag should be attached to a sequence encoding a desired protein for purposes of identifying or purifying the desired protein upon translation. Rothchild, however, fails to remedy the deficiencies of Lanar '949 in describing the other aspects of the instant invention and therefore the combination of Lanar with Rothschild fails to disclose or suggest every element of the invention as claimed.

Accordingly, the Examiner fails to establish *prima facie* obviousness of the invention by the combined references and the instant rejection should be withdrawn.

Applicants submit that the present application well-describes and claims patentable subject matter. Accordingly, the favorable actions of withdrawal of the standing rejections and allowance of the application are respectfully requested.

In the event that there are minor issues precluding allowance of the application that can be addressed by a telephone discussion, the Examiner is invited to call the undersigned at 703-205-8043 .

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Respectfully submitted,

By _____

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Attachment: Replacement Sheet of Fig. 4

English translation of Kigawa reference (Protein, Nucleic Acid and Enzyme , Vol. 47, No. 8, 2002)

Amended copy of PTO-1449 filed with IDS on November 23, 2004

DRN/mua

Amendment to the Drawings

Attached hereto is one (1) sheet of corrected formal drawing that complies with the provisions of 37 C.F.R. § 1.84. The corrected formal drawing incorporates the following drawing changes:

The Examiner has objected to Figure 4 as not being legible. In a telephone interview with the Examiner, it was clarified that the corrected Figure 4 filed with Applicants previous response was received by the Examiner as a blank, black field. Applicants provide herewith a reprinted Figure 4 (replacement sheet showing Figure 4).

It is respectfully requested that the corrected formal drawings be approved and made a part of the record of the above-identified application.

Attachment: Replacement sheet of Fig. 4